

Application No. : 10/713,479

Responsive to an Office Action mailed May 30, 2006 and a Notice of a Noncompliant Amendment mailed November 21, 2006

Response filed December 14, 2006

REMARKS

Claims 1–12 and 14–45 are pending. Claims 19–35 have been withdrawn. Applicants thank Examiners Crowe and Switzer for the courtesy of the interview with the Applicants' attorney conducted on October 17, 2006.

A Notice of Noncompliant Amendment was mailed November 21, 2006, citing to non-compliant claim status identifiers. In response, the status identifier of claim 19 has been corrected to --Withdrawn--currently amended--, and the status identifiers of claims 2–12 and 14–18 have been corrected to -- Currently amended--. There are no substantive changes in this paper.

Amendments to the Claims

Although Applicants believe that the rejected claims are allowable over the references of record, some of the claims have been amended to expedite prosecution. As such, Applicants do not acquiesce to the Examiner's characterizations of the claims and/or references not specifically traversed herein.

Claim 1 has been amended to incorporate the subject matter of claim 13. Accordingly, claim 13 has been canceled. In claims 1–12 and 14–18, the term "system" has been replaced by "apparatus" as suggested by the Examiner.

Claim 1 has been amended to recite that the photoelectrochemical label is "selective for non-covalently binding double-stranded nucleic acids over single-stranded nucleic acids." Support for this amendment is found, for example, in ¶ [0048] of the specification. Applicants submit that this amendment is simply clarifying and does not change the scope of the claim.

Claim 1 has been amended to recite that the light source is "of sufficient energy and intensity to initiate a photoelectrochemical reaction of the non-covalent photoelectrochemical label." Support for this amendment is found, for example, in ¶ [0024] of the specification. Applicants submit that this amendment is simply clarifying and does not change the scope of the claim.

Claim 18 has been amended to incorporate the amendments to claim 1.

Claims 31, 36–45 have been canceled without prejudice. Applicants reserve the right to pursue the subject matter of these claims in continuing applications.

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Claim Rejections Under 35 U.S.C. § 112

Claims 1–18 stand rejected under 35 U.S.C. § 112, second paragraph as indefinite. The Examiner states that it is unclear how the recitation of “a non-covalent photoelectrochemical label for contacting with the nucleic acid probe” defines structural limitations of the recited system. Claim 1 has been amended to recite in part “a non-covalent photoelectrochemical label *selective for binding double-stranded nucleic acids over single-stranded nucleic acids* for contacting with the nucleic acid probe.” This amendment structurally links the non-covalent photoelectrochemical label to the nucleic acid probe through the recitation of “binding.” Accordingly, Applicants submit the rejection is overcome.

Furthermore, M.P.E.P. 2172.01 provides that “A claim does not necessarily fail to comply with 35 U.S.C. 112, second paragraph where the various elements do not function simultaneously, are not directly functionally related, do not directly intercooperate, and/or serve independent purposes.” *Ex parte Huber*, 148 U.S.P.Q. 447, 448–49 (Bd. Pat. App. 1965). Applicants submit that the recitation of “a non-covalent photoelectrochemical label for contacting with the nucleic acid probe” is not indefinite under *Ex parte Huber* and request withdrawal of the rejection.

Claims 13 and 14 stand rejected under 35 U.S.C. § 112, second paragraph as indefinite. The Examiner states that it is unclear how the recitation of “a sacrificial reductant” defines structural limitations of the recited system. Again, Applicants submit that the recitation of “a sacrificial reductant” is not indefinite under *Ex parte Huber* and request withdrawal of the rejection. Because claim 1 has been amended to incorporate the subject matter of claim 13, Applicants submit that this rejection would also be inapplicable to claim 1 as amended for the same reason.

Claim Rejections Under 35 U.S.C. § 102

“A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.” *Verdegaal Bros. v. Union Oil Co.*, 814 F.2d 628, 631, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987).

Rejections over Hashimoto. Claims 1, 2, 4, 6–10, and 13–17 stand rejected under 35 U.S.C. § 102(b) as anticipated by Hashimoto (U.S. Patent No. 5,776,672). Applicants submit that

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Hashimoto does not anticipate claim 1 because there is no identity of invention between Hashimoto and claim 1. "Identity of invention is a question of fact, and one who seeks such a finding must show that each element of the claim in issue is found, either expressly or under principles of inherency, in a single prior art reference, or that the claimed invention was previously known or embodied *in a single prior art device or practice*." *Minnesota Min. & Mfg. v. Johnson & Johnson*, 976 F.2d 1559, 1565, 24 U.S.P.Q.2d 1321 (Fed. Cir. 1992) (emphasis added). M.P.E.P. 2131 is in accord: "The elements must be arranged as required by the claim." *In re Bond*, 910 F.2d 831, 15 U.S.P.Q.2d 1566 (Fed. Cir. 1990).

The Examiner has assembled the features of claim 1 by picking and choosing from different systems for gene detection disclosed in Hashimoto. Hashimoto discloses at least two different systems for detecting a gene, optical and electrochemical, each of which includes one or more components not present in the other. Hashimoto does not disclose, either explicitly or implicitly, a single system comprising *all* of the features recited in claim 1. Accordingly, there is no identity of invention between claim 1 and Hashimoto and Hashimoto does not anticipate claim 1 for at least this reason.

For example, the Examiner characterizes luciferin and H₂O₂ in Example 12 as the light source recited in claim 1. Hashimoto at 20:23–53. Example 12 describes an optical detection method, and as such, lacks several features recited in claim 1. In this example, an oligonucleotide probe is immobilized to the surface of an optical fiber, through which an optical signal is detected. The optical fiber in Example 12 is not an "electrode," as recited in claim 1. Because Example 12 uses optical detection, the disclosed system also does not comprise the "data collection controller for measuring a current at the electrode" recited in claim 1. Similarly, Hashimoto does not disclose an embodiment using electrochemical detection that comprises a light source.

Moreover, Hashimoto does not disclose every feature recited in claim 1. Claim 1 has been amended to incorporate the subject matter of claim 13, and now recites in part "a sacrificial reductant suitable for contacting with the nucleic acid probe." In rejecting claim 13, the Examiner refers to the disclosure of distearylaminodimethyl ammonium chloride, a salt of a tertiary amine (Hashimoto at 11: 14–19) as inherently including the function of the sacrificial reductant. It is not

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entirely clear to what compound “distearylaminodimethyl ammonium chloride” refers, since the specification states that it is an ammonium salt, but the name also includes the term “amine.” Applicants believe that the compound in question is actually “distearyldimethylammonium chloride” because this compound is recited in a similar passage of the specification for the same purpose (preventing non-specific adsorption). Hashimoto at 10:12–15.

Distearyldimethylammonium chloride does not function as a sacrificial reductant. Exhibit A attached hereto is a copy of page 81 of Lowe, Lisa Bizzell “Synthesis and Characterization of a Dye Sensitizing Molecule for Photoelectrochemical DNA Hybridization Detection” Masters Thesis, North Carolina State University, July 2002, page 55 to end, which was disclosed in an IDS filed on February 13, 2004. As explained in the text and illustrated in *Eq. 4.2*, the sacrificial reductant tripropylamine (Pr_3N , TPA) is believed to first undergo a one-electron oxidation from a non-bonded electron pair to form a tripropylamine radical cation. Because distearyldimethylammonium cation, a quaternary ammonium cation, does not have a non-bonded electron pair, it cannot undergo the illustrated single electron oxidation. Consequently, distearyldimethylammonium chloride does not function as a sacrificial reductant as recited in claim 1.

Moreover, distearyldimethylammonium cation and the other compounds in the cited portion of Hashimoto, for example, sterylamine and aminononadecane, are used to coat a carrier on which nucleic acids are immobilized in order to prevent non-specific absorption during an assay for a target DNA sequence. Hashimoto at 10:62–11:20. This coating apparently is stable to the conditions under which the assay is performed, for example, at “from 37° to 72°” in water. Hashimoto at 13:1–4. The coating is also apparently stable to conditions under which a hybridized target nucleic acid sample is dissociated when regenerating the sensor, for example by treatment “with heat, bases, acids, surfactants or ultrasonic wave.” Hashimoto at 13:61–14:3. Exemplary conditions include heating to 98° C, treatment at pH 8.5 or higher, treatment at pH 4.5 or lower, treatment with surfactant at 0.1% or higher, ultrasound at from 10–100 kHz. Hashimoto at 14:3–16. These compounds do not function as sacrificial reductants because they are apparently immobilized on the surface of the carrier, and consequently, unable to donate electrons to a non-covalent photoelectrochemical label in contact with a nucleic acid probe as

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recited in claim 1. Accordingly, Hashimoto does not disclose a sacrificial reductant as recited in claim 1.

During the interview, the Examiner mentioned Hashimoto's disclosure of EDTA, noting that pending claim 14 recites EDTA as a sacrificial reductant. Hashimoto discloses releasing nucleic acid from cells using EDTA. Hashimoto at 12:28-33. The nucleic acid, at this stage double-stranded, is bound to a support. Hashimoto at 12:37-39. The supported nucleic acid is then washed "to remove unnecessary components," after which the double stranded nucleic acid is released from the support. Hashimoto at 12:42-46. At this point, the double stranded nucleic acid is free of any non-nucleic acid cell components and lysing agents, for example, EDTA. The double-stranded nucleic acid is then denatured into single-stranded nucleic acid. Hashimoto at 12:64-67. An electrode to which a nucleic acid probe has been immobilized is then contacted with the single-stranded nucleic acid. Hashimoto at 12:67-13:4. Accordingly, in Hashimoto, the nucleic acid probe never contacts EDTA. For the reasons discussed above, because Hashimoto does not disclose an embodiment comprising EDTA in combination with a nucleic acid probe, there is no identity of invention between Hashimoto and claim 1.

Applicants submit that claim 1 is not anticipated by Hashimoto for at least the reasons provided above. Because claims 2, 4, 6-10, and 14-17 are dependent on claim 1, these claims are also not anticipated by Hashimoto for at least the same reasons. Nor would claims 1, 2, 4, 6-10, and 14-17 be obvious over Hashimoto for at least the reason that Hashimoto does not disclose or suggest every feature recited in claim 1.

Rejections over Stanley. Claims 36, 37, and 40 stand rejected under 35 U.S.C. § 102(b) as anticipated by Stanley (U.S. Patent No. 5,824,477). Because claims 36, 37, and 40 have been canceled, this rejection is moot.

Rejections over Wohlstadter. Claims 36-37 and 41-44 stand rejected under 35 U.S.C. § 102(b) as anticipated by Wohlstadter (U.S. Patent No. 6,207,269). Because claims 36-37 and 41-44 have been canceled, this rejection is moot.

Rejections Under 35 U.S.C. § 103

A *prima facie* rejection for obviousness requires: (1) a disclosure or suggestion of every element of the claim in the cited reference or references; (2) a suggestion or motivation to modify

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or combine the references; and (3) a reasonable expectation of success. The suggestion to combine and the reasonable expectation of success must be found in the cited references or known to one skilled in the art. *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991). Applicants submit that the cited references do not disclose or suggest every feature recited in the claims, and that the Examiner has not shown either a reasonable expectation of success in combining the references.

Rejections over Hashimoto and Gillespie. Claims 3 and 5 stand rejected under 35 U.S.C. § 103(a) as unpatentable over Hashimoto in view of Gillespie (U.S. Patent No. 5,482,834). Claims 3 and 5 are dependent on claim 1. The Examiner relies on Hashimoto for the disclosure of the features of claim 1, and relies on Gillespie only for disclosing RNA. As discussed above, Hashimoto does not disclose every feature recited in claim 1. Moreover, Gillespie does not appear to disclose a non-covalent photoelectrochemical label suitable for labeling double-stranded nucleic acids comprising RNA. Because the cited references do not disclose or suggest every feature recited in claims 3 and 5, these claims are not obvious over the cited combination for at least these reasons.

The Examiner provides as a motivation to combine Hashimoto with Gillespie, “allowing measurement of variations in expression of genes as explicitly taught by Gillespie.” The Examiner’s alleged motivation does not link Gillespie to Hashimoto in any way, and as such, the rejection is improper and should be withdrawn for at least this reason.

Rejections over Hashimoto and Dabiri. Claim 11 stands rejected under 35 U.S.C. § 103(a) as unpatentable over Hashimoto in view of Dabiri (U.S. Patent No. 5,871,628). Claim 11 is dependent on claim 1. The Examiner relies on Hashimoto for the disclosure of the features of claim 1, and relies on Dabiri only for disclosing a laser light source. As discussed above, Hashimoto does not disclose every feature recited in claim 1.

Dabiri appears to disclose an imaging spectrograph system for slab-gel DNA sequencing. The Examiner refers to electrodes disclosed at col. 3, ll. 65–67. Dabiri does not disclose or suggest attaching nucleic acids thereto. The Examiner also refers to fluorescent dyes. Dabiri at 7:30–36. Dabiri does not disclose or suggest that these dyes are useful as non-covalent photoelectrochemical labels. The dyes are apparently covalently bound to the DNA fragments.

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See, for example, Dabiri at 4:17–19 (“First, DNA fragments that are tagged with fluorescent dyes are produced. The dyes indicate an end base associated with the respective DNA fragment.”). Furthermore, Dabiri does not disclose or suggest that the dyes are photoelectrochemically active. Because Hashimoto and Dabiri do not disclose or suggest every feature recited in claim 11, claim 11 is not obvious over the cited combination for at least this reason.

The Examiner provides as a motivation to combine Hashimoto with Dabiri, “providing frequencies compatible with a wide variety of fluorescent dyes as explicitly taught by Dabiri.” The Examiner’s alleged motivation does not link Dabiri to Hashimoto in any way, and as such, the rejection is improper and should be withdrawn for at least this reason.

Rejections over Hashimoto and Noblett. Claim 18 stands rejected under 35 U.S.C. § 103(a) as unpatentable over Hashimoto in view of Noblett (U.S. Patent No. 6,362,004). Claim 18 is dependent on claim 1. The Examiner relies on Hashimoto for the disclosure of the features of claim 1, and relies on Noblett only for disclosing machine readable identifying indicia. As discussed above, Hashimoto does not disclose every feature recited in claim 1. Because Hashimoto and Noblett do not disclose or suggest every feature recited in claim 18, claim 18 is not obvious over the cited combination for at least this reason.

Rejections over Hashimoto and Wohlstadter. Claims 36–37 and 39–44 stand under 35 U.S.C. § 103(a) as unpatentable over Hashimoto in view of Wohlstadter. Because claims 36–37 and 39–44 have been canceled, this rejection is moot.

Rejections over Hashimoto, Wohlstadter, and Gillespie. Claim 38 stands rejected under 35 U.S.C. § 103(a) as unpatentable over Hashimoto in view of Wohlstadter, and further in view of Gillespie. Because claim 38 has been canceled, this rejection is moot.

Rejections over Hashimoto, Wohlstadter, and Noblett. Claim 45 stands rejected under 35 U.S.C. § 103(a) as unpatentable over Hashimoto in view of Wohlstadter, and further in view of Noblett. Because claim 45 has been canceled, this rejection is moot.

Rejoinder of Withdrawn Claims

Because the pending claims are allowable over the art of record, Applicants request rejoinder of the withdrawn claims and examination of the same under M.P.E.P. 821.04, which provides for rejoinder of any claim that requires all the limitations of an allowable claim.

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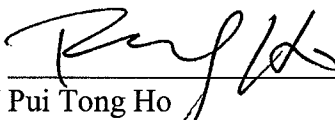
Because withdrawn claims 19-30 and 32-35 recite every feature of claim 1, Applicants request rejoinder of these claims.

Applicants submit that all claims are now allowable over the reference of record for at least the reasons provided above. Applicants believe that the amendments and arguments provided in this paper are sufficient to overcome all of the Examiner's outstanding rejections. Applicants have not presented every possible reason that the pending claims are allowable over the cited references, and as such, do not acquiesce to any of the Examiner's characterizations of the pending claims, characterizations of the cited references, or arguments not specifically traversed. If the Examiner believes that any outstanding issues remain that may be resolved in a telephonic interview, the Examiner is invited to contact the undersigned. Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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